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RADIATION THERAPY OF CARCINOMA OF THE CERVIX UTERI*

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IRRADIATION, as the exclusive treatment in carcinoma of the cervix, has always played an important part in the treatment of this disease and has been practiced for many years. Methods have changed in the course of time and various centers have worked out different treatment methods. Time does not permit a discussion of all these; but it is really unnecessary, as the underlying principles are the same in all these methods, regardless of differences in details. As a guide in explanation of what we want to achieve, and how we proceed, I shall outline the treatment approach as it is used at the Francis Delafield Hospital of New York. But first, I would like to summarize a few well-known factors.

In order to treat carcinoma of the cervix successfully with irradiation, it is necessary to deliver a high destructive dose to the primary tumor in the cervix and a somewhat lesser, but still considerable dose throughout the pelvis, in order to give to the parametria and lymph nodes also a sufficiently high dose. Radium and external radiation must

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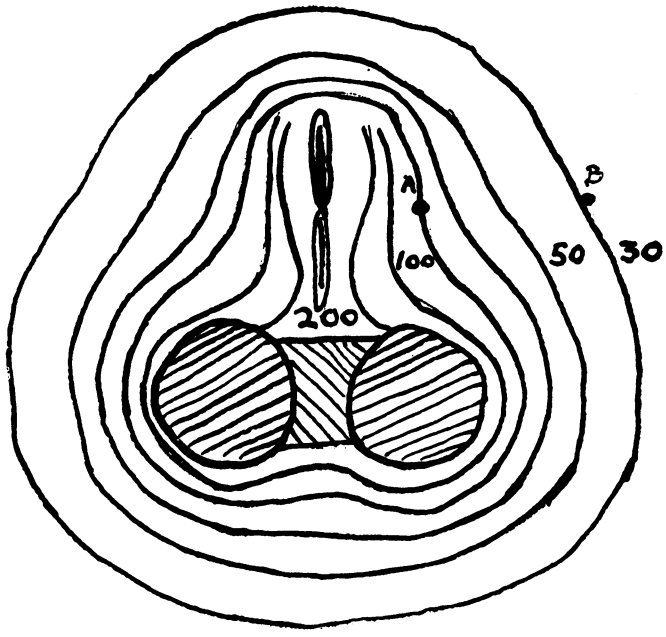

Fig. 1

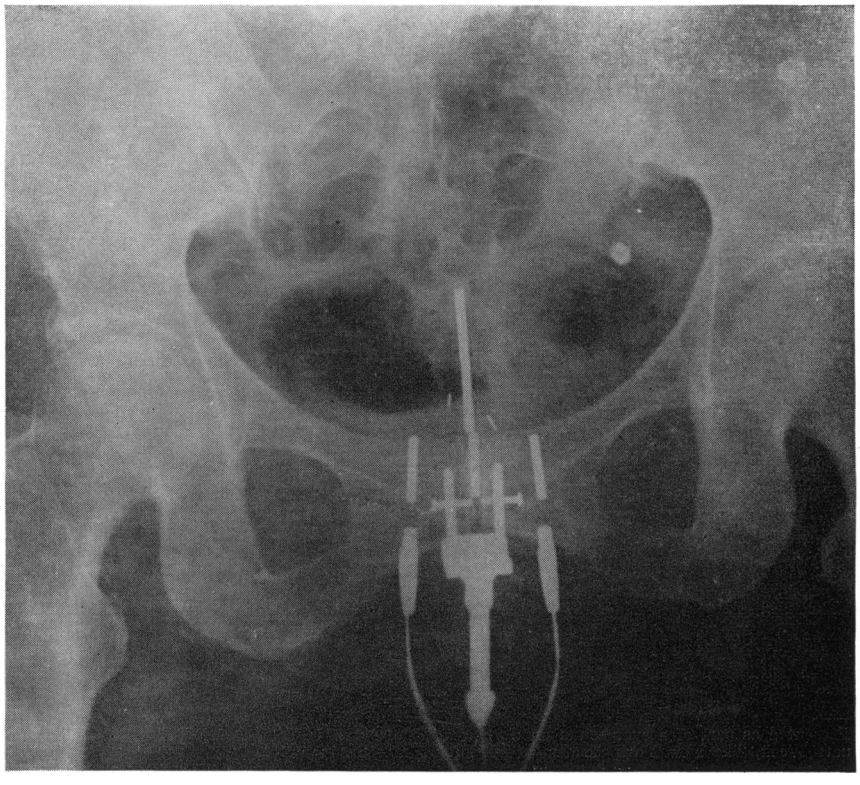

Fig. 2

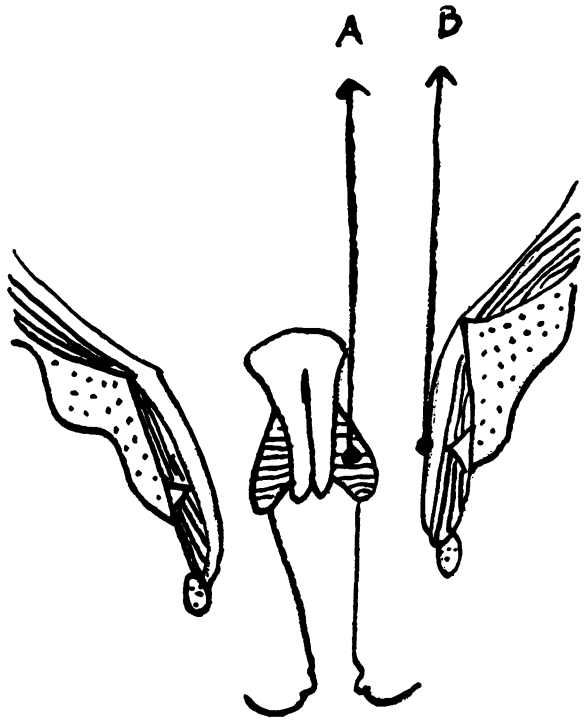

Fig. 3

be combined in order to achieve this goal; neither of the two is sufficient in itself. Radium is most effective at the area of contact, but loses its effect rapidly at relatively short distances from this point. Figure 1 shows the dosage readings around a group of applicators as they are used in the treatment of carcinoma of the cervix and shows the fall-off of the dosage from 200 gamma roentgens at the center to 100 r at 2 cm. and 30 r at 5 cm. distances from the sources.

This physical quality must limit the use of radium to the treatment of the primary tumor, while the treatment of the parametria, lateral pelvic walls and node-bearing areas must be carried out by external radiation. The cervix proper tolerates a tremendous amount of radiation, but our limitations lie in the close proximity of bladder, rectum, small intestine and ureters; and it is on account of these healthy neighboring organs that our dosage has to be worked out very carefully so that we can give a dose which is sufficient to destroy the disease without impairing healthy tissues beyond repair. This represents a difficulty, as the

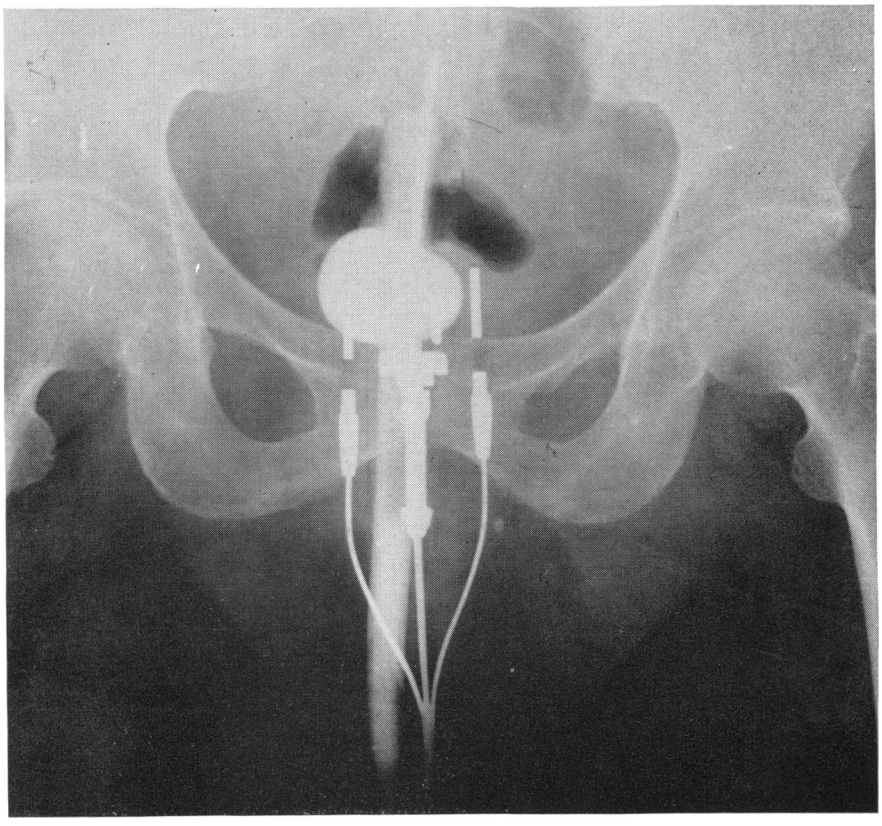

Fig. 4

sensitivity of healthy tissues and carcinomatous tissues to irradiation differs only in degree, which leaves a very slim margin of safety.

To return now to the actual procedure in the treatment of carcinoma of the cervix, I shall start with a discussion of the use of radium. Various applicators have been designed to distribute the radium effectively. Among the best known are the Stockholm, Manchester, Corscaden and Ernst applicators. They all follow about the same principle and are equally useful in the hands of the expert. We are currently using the Corscaden applicator, but occasionally use the Manchester ovoids. Figure 2 shows the roentgenogram of a patient with a Corscaden applicator in place. In this patient the applicator is loaded with 30 mg. of radium, in tandem, which has been introduced into the cervical canal; 20 mg. in each of the plugs are placed against the vaginal fornices, and 10 mg. is placed directly against the cervix. This amount

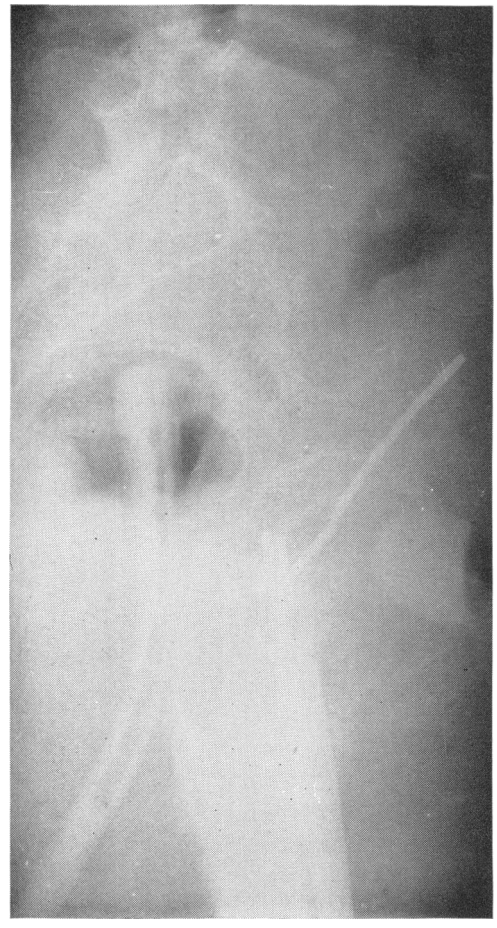

Fig. 5

of radium is left in place twice for 36 hours. The actual radium dose is calculated in each patient.

With the use of such a radium application, we aim to deliver to the cervix proper a dose which is tremendous, namely, 12,000 gamma roentgens. But in the paracervical triangle, the area which is known as Point A, and which is 2 cm. above and 2 cm. lateral to the cervical os, the delivered dosage is only 6,000 r, and at Point B, which is at the same level but 3 cm. further lateral, the dose has decreased to 2,000 r (Fig. 3).

These figures demonstrate clearly that the radium application which is so effective at the point of contact, needs a supplementary dose beyond this point. It is also clear that, if the radium is not in an ideal

position, we will not only be unable to get the desired beneficial effect, but will have undesirable side effects. The precautions taken in attempting to avoid such side effects include the following: we take direct readings with a small ionization chamber, the Bomke dosimeter, which, when introduced into the rectum and the bladder of the patient in the operating room, will indicate to us the permissible amount of radiation which these organs will receive. As a second precautionary measure we take films with the radium in place. Figures 4 and 5 show the Corscaden applicator in place and, in addition, show a tube in the rectum and some contrast media in the bladder. They clearly show that there is a safe distance between the radium and these organs. However, if the films should show that the position of the radium is not entirely satisfactory, or if the readings with the Bomke dosimeter are too high, the radium is removed and reintroduced, and if improvement is impossible, as is sometimes the case, due to anatomical difficulties, the dosage must be reduced. Accuracy in each step of the procedure is of utmost importance, not only for success in treatment, but for the avoidance of complications.

We prefer to start the combined treatment course with the radium, at least in patients with tumors at Stages I and II. In those with Stage III we believe it is better to start with external radiation, in order to restore, in some degree, the normal anatomy before trying to apply the radium. Some clinics prefer to start treatment with external radiation and follow it with radium therapy. There are, of course, pros and cons associated with each of the two methods, but we feel that by using the radium first, and thereby delivering a decisive blow to the tumor, we have gained an important advantage.

The course of external radiation therapy is begun ten days after the completion of the radium therapy. It is our aim to deliver a uniform dose of 4,000 r throughout the pelvis, and we do this with one of our supervoltage units, namely, a 2-MV Unit, at the rate of 200 r TD (tumor dose) daily. The course of external therapy lasts about four weeks; the entire treatment time, combining radium and external therapy, about eight weeks. When external radiation is given, the rays must pass through healthy surrounding organs and tissues in order to reach the diseased area. Although our objective is to destroy cancer cells beyond repair, we must, at the same time, give healthy cells which are in the path of radiation a chance to survive. In such a situation, it is obvious that

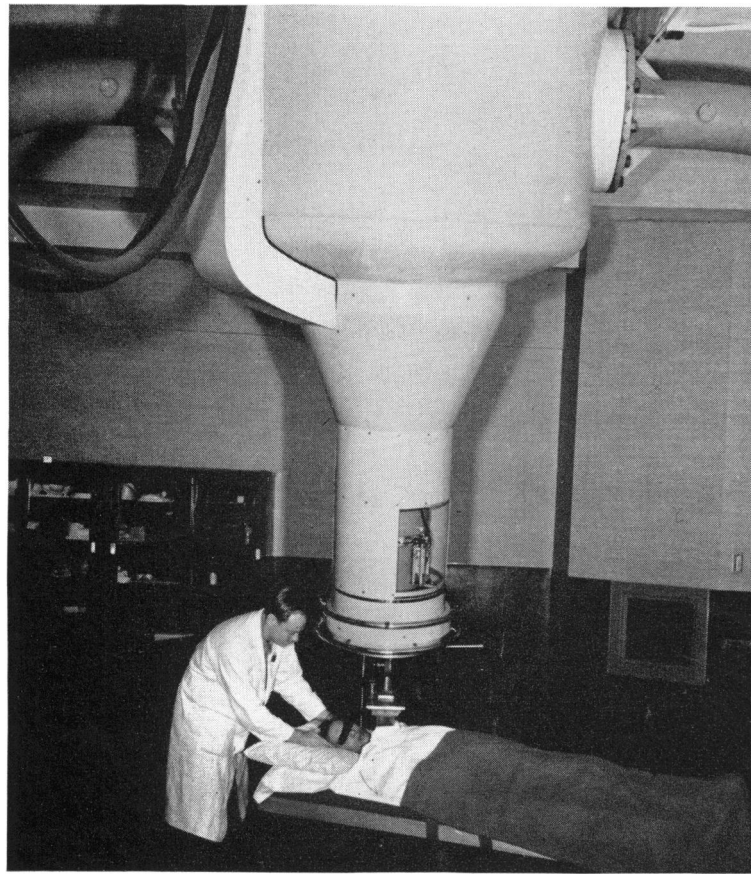

Fig. 6

problems will arise. We must realize that these healthy cells will unavoidably show a certain amount of radiation damage. The question then arises: how is it possible to perform this task at all? The answer lies in the fact that there is a difference in the sensitivity of the normal and of the tumor cell to radiation. The tumor cell is more sensitive to radiation than the normal one, and it is this degree of difference in radiosensitivity between the two which determines our success in the treatment of any malignant disease with irradiation. If we plan our treatments carefully and take advantage of this difference in sensitivity, we can often achieve satisfactory results.

Supervoltage therapy has made this difficult task much easier. Deep x-ray machines, ranging between 200 and 250 KV, have been used for many years in the treatment of deep-seated malignant tumors, but

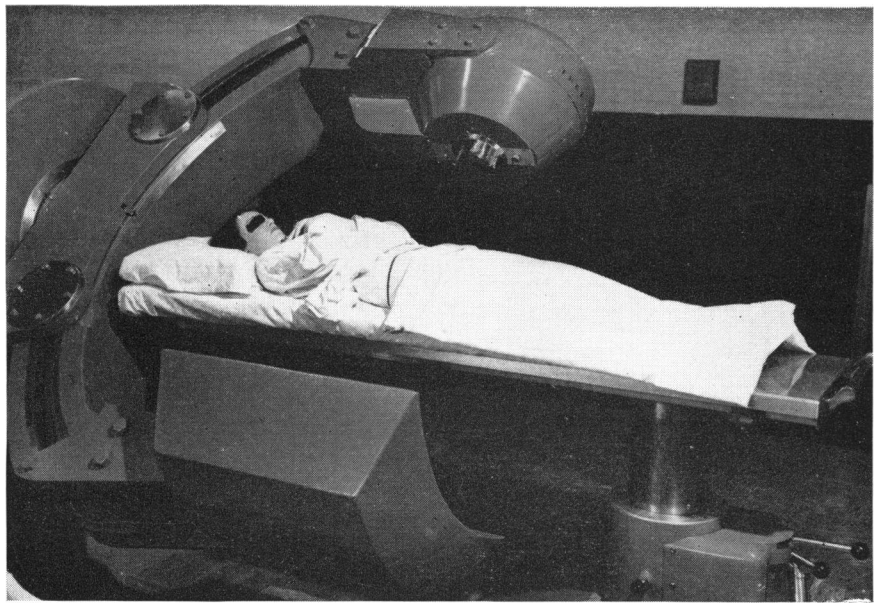

Fig. 7

TABLE I.—PERTINENT PHYSICAL QUALITIES OF THE 2-3 MV IRRADIATION

1. Better penetration.
2. Maximum ionization not on the surface but 0.4 cm. below.
3. Decreased absorption of the radiation and cartilage; and
4. Diminished side scatter.

during recent years, supervoltage units of or above 1000 KV have been used more and more for the external treatment of deep-seated cancers. I shall discuss briefly their mode of action and their advantages. To make the point of disillusionment first, supervoltage therapy is not a "miracle" weapon. The biological effect on the cell is essentially the same regardless of whether voltages in the range of 1-6 MV or in the range of 200-250 KV are employed. However, with the higher voltages in the Betatron range, the biological effect is approximately 10 per cent less than when 250 KV therapy is used. I shall discuss only the qualities of the supervoltage units, which are now mainly used, namely, the 2-MV unit and the CO-60 unit, which is equivalent to a 3-MV machine (Figures 6 and 7).

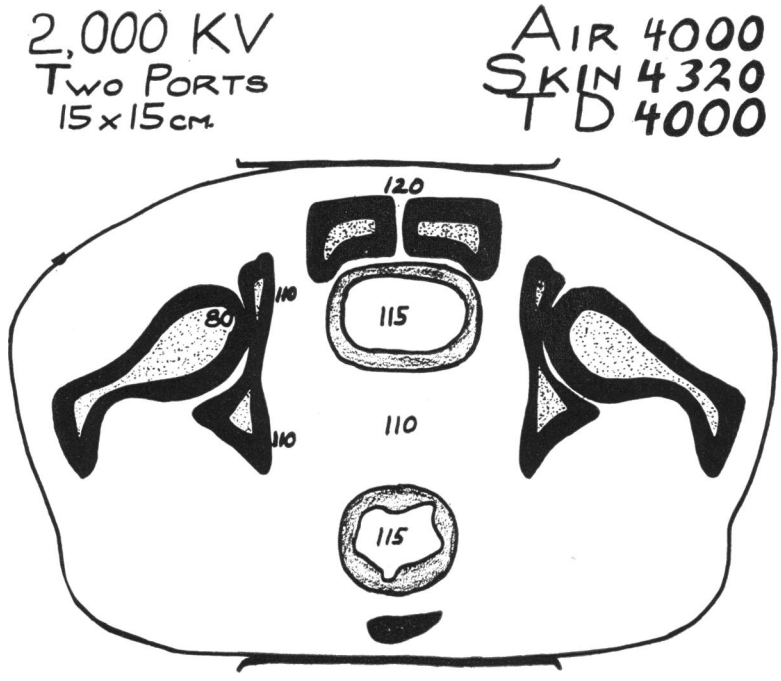

Fig. 8

May I repeat: the biological effect of a supervoltage unit is essentially the same as that of a deep x-ray machine. If, therefore, advantages can be expected with the use of the hard beam of radiation, which is typical of supervoltage units, they must be due to better physical qualities. These superior physical qualities do indeed exist and they are exclusively responsible for the usefulness of the machines (Table I). All of these different physical qualities result in the ability to give a higher tumor dose with less damaging side effects, since the local and general tolerance to therapy is improved due to these physical qualities.

We treat the patient on the 2-MV unit through two opposing fields (Figure 8). The desired tumor dose of 4000 r is delivered with a skin dose of 4300 r, which is well tolerated when supervoltage is used. A central lead shield protects bladder and rectum. An approach as easy and effective as this is not possible with conventional deep x-ray therapy. In order to get the desired tumor dose with these units, a different approach must be used, namely, through multiple fields, crossfiring at the lesion; otherwise the dose to skin and underlying tissues would be higher than healthy tissues can tolerate (Figures 9 and 10).

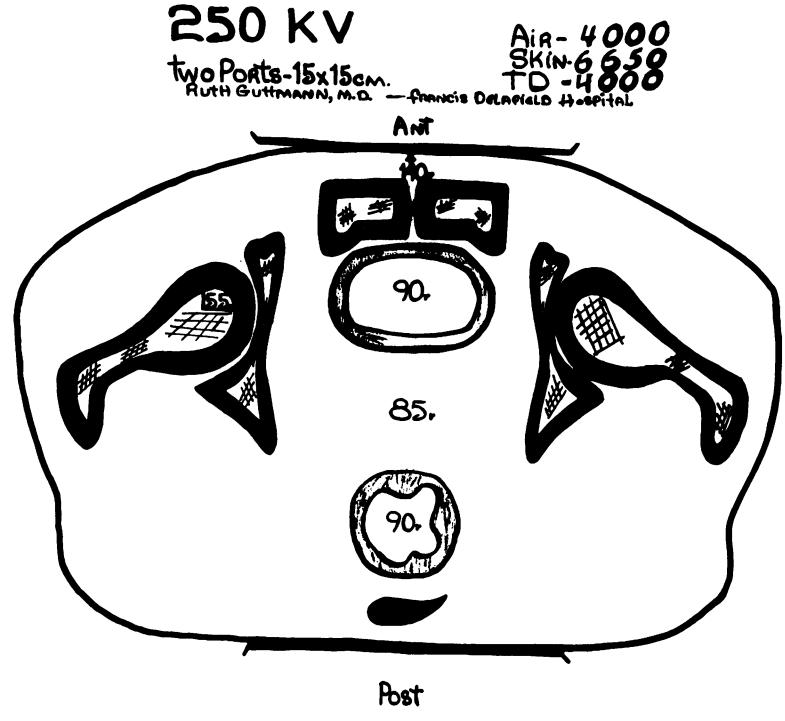
250 KV
two Ports-15x15cm.
Ruth Guttmann, M.D. — Francis Delafield Hospital
Air - 4000
Skin 6650
TD - 4000
Ant
90.
85.
90.
Post

Fig. 9

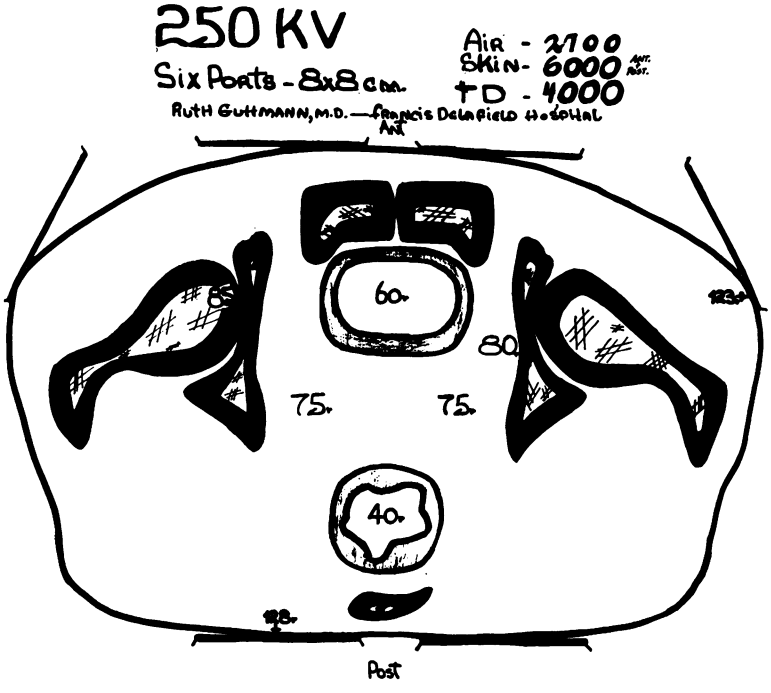
250 KV
Six Ports - 8x8 cm.
Ruth Guttmann, M.D. — Francis Delafield Hospital
Air - 2100
Skin - 6000
TD - 4000
Ant
60.
80.
75.
75.
40.
Post

Fig. 10

TABLE II.—RESULTS—CARCINOMA OF CERVIX
Radiumhemmet, Stockholm — 1949/50

	No. of Cases	*Alive*
Stage I	109	89.9%
Stage II	388	53.3%
Stage III	145	28.7%
Stage IV	60	10%
	702	50.1%

Again, as in the treatment with radium, we try to be as accurate as possible, because even a near-miss will impair results. In outlining the field for external radiation, we must make certain that all the areas which we want to have included in the field of irradiation are actually included. For this purpose, measurements of each patient are taken, a cross-section of the pelvis is put on paper, the tumor dose is calculated for each individual, and localization films are taken. These films are taken on the treatment table with the treatment machine and with the patient in the proper treatment position. They are not diagnostic films, but they give us the desired information and it is important to take them under actual treatment conditions, as a deviation of 2 to 3 cm. may make the difference between unnecessarily including some vital areas in the field of irradiation or excluding them from it.

The approach to treatment of Stage IV carcinoma of the cervix uteri is somewhat different. If a patient has a far-advanced cervical lesion which has invaded bladder or rectum, an approach with external radiotherapy alone is carried out. Further therapy is planned according to the response of the disease and shaped to the situation which develops after the course of external therapy. If, on the other hand, a patient is classified as Stage IV due to distant metastases, for instance supraclavicular metastases, while the local lesion is not too advanced, then one might carry out the treatment plan appropriate for a less advanced local lesion and treat the distant metastases separately.

Results in the treatment of carcinoma of the cervix with irradiation vary with the different stages. It is, therefore, fallacious to try to express average results with figures which include all stages, I through IV. Obviously, such results will be greatly influenced by the incidence of those with early or late stages in such a group. By the same token, I feel

TABLE III.—DISTRIBUTION OF POSITIVE NODES IN PATIENTS AFTER SUPERVOLTAGE THERAPY

From The Francis Delafield Hospital and the Columbia-Presbyterian Medical Center, New York

	Number of Cases	*Number of Positive Nodes*
Stage I	28	0
Stage II	23	1
Stage III	5	2

that only statistics that include a large number of patients give a valid impression of the value of a method. Kottmeier published his results in a series of 700 patients with carcinoma of the cervix whom he treated with radium and conventional radiotherapy between 1949 and 1950 (Table II).

Others have been able to publish similar results in somewhat smaller patient groups. These results of irradiation were achieved when radium and conventional radiotherapy were combined, that is, radiation ranging between 200 and 250 KV; and the question is appropriately asked whether these figures have been improved by the use of supervoltage therapy. We have treated a large group of patients with supervoltage therapy at the Francis Delafield Hospital but, unfortunately, a large percentage of these patients has had previous therapy, either surgery or radiotherapy, and therefore cannot be used for evaluation. However, Fletcher* of the M. D. Anderson Hospital in Houston, Texas has had the opportunity to treat a very large group of patients with carcinoma of the cervix and has been able to supply us with comparative data. In his institution he treated simultaneously a group of 505 patients with standard procedures, that is, with radium and conventional x-ray therapy, and 672 patients with radium and supervoltage pelvic irradiation. He found that the proportion of five-year survivals in the late Stage II and Stage III cancers rose 10 per cent when supervoltage therapy was used. This improved five-year survival rate in these advanced cases is, without doubt, due to the ability to sterilize the involved lymph nodes with high dosages which can be used with this type of radiation. Some work which has been carried out at the Francis Delafield Hospital bears this out quite well. For some years in the past, lymph node dissections were performed on patients who were treated with irradiation for car-

* Personal Communication.

TABLE IV.—COMPARATIVE FIGURES OF DISTRIBUTION OF POSITIVE NODES AFTER SUPERVOLTAGE THERAPY AND AFTER RADICAL HYSTERECTOMY

	To be expected according to the literature	*Our material*
Stage I	17 out of 100	0 out of 28
Stage II	31 out of 100	1 out of 23

cinoma of the cervix, whenever the primary disease was controlled. This plan was carried out for some years; it has now been abandoned but the patient-material which was treated in this way has given us important information (Tables III and IV).

These tables show quite clearly one reason why we have given up performing radical lymph node dissections after radiotherapy. Positive nodes were found in a very small number of patients, and these patients died from their disease in spite of the surgical procedure. Included in this group of patients is one very interesting case of a woman with carcinoma of the cervix, Stage III. This patient was scheduled to be treated with surgery. However, the operation was abandoned because of the presence of positive lymph nodes which were proven by biopsies; instead, the patient was treated with irradiation. The primary disease was controlled and she underwent a lymph node dissection four months later. Most careful microscopic screening of the nodes did not show any evidence of the disease and the patient is alive eight years after radiotherapy.

The use of supervoltage therapy is essential in the sterilization of nodes because it is, in my opinion, necessary to deliver a total dose of 5000 r, which is technically very difficult with conventional therapy and can be done only with the more penetrating beam of supervoltage therapy.

No presentation of the treatment of carcinoma of the cervix with irradiation is complete without mentioning complications resulting from this treatment. Due to the proximity of bladder, ureters, rectum and small bowel, most of the complications can be expected to occur in these organs and, indeed, late side effects do occur. In a group of 301 patients whom I have treated with conventional therapy, vaginal cones and radium, I have found late side effects in either bladder or rectum

in 15 per cent. However, serious complications occurred in only 2 per cent of this group. On the other hand, more serious complications, especially those involving the small bowel, have occurred in a patient group which was treated with radium and supervoltage therapy, especially when this type of irradiation and a surgical procedure were combined. I have already mentioned one reason why we have given up lymph node dissections in patients who have received a full cycle of radiotherapy. If the operation had proved useful, we would have been forced to alter our approach, as the complication rate was highest when the two methods were combined. This is easy to explain, as the blood supply is greatly altered by aggressive radiotherapy, and is again disturbed by an extensive surgical procedure, often causing severe and irreparable damage.

It has also been our experience that the incidence of complications is higher in patients who suffer from inflammatory intestinal diseases, such as diverticulitis or diverticulosis, and in those who have had previous surgical procedures which have resulted in the small bowel being tied down by adhesions and thus being exposed to more intensive radiation than is a freely movable small bowel. We also believe that there are racial differences in the tolerance to radiation; that, in underprivileged patient groups and in patients who suffer from sprue-like vitamin deficiencies, radiation reactions are more severe. One should realize, however, that when dealing with an aggressive disease, aggressive treatment methods are required, and some side effects are unavoidable, even when the greatest care is taken. They must be accepted as a calculated risk.

In closing, I would like to point out that treatment exclusively with radium and external radiotherapy has produced excellent results in the treatment of carcinoma of the cervix, when it is carried out with a full understanding of the problems involved, and with the necessary accuracy and care.

Radiotherapy has played and continues to play an important role in the treatment of this disease, where it remains one of our most important and trusted weapons.